13. (amended) A plant transformation vector which comprises a [modified] disarmed plant tumor inducing plasmid of *Agrobacterium tumefaciens* [which is capable of inserting] and a chimeric gene [into susceptible plant cells], wherein the chimeric gene [comprises] contains a promoter from cauliflower mosaic virus, said promoter selected from the group consisting of a CaMV(35S) promoter and a CaMV(19S) promoter and a structural sequence which is heterologous with respect to the promoter.

Please amend claim 16 to read as follows:

16. (amended) A differentiated dicotyledonous plant comprising plant cells [which express a polypeptide by steps comprising transcription of] containing a chimeric gene which comprises a promoter from cauliflower mosaic virus, said promoter selected from the group consisting of a CaMV(35S) promoter and a CaMV(19S) promoter, and a structural sequence [encoding said polypeptide] which is heterologous with respect to the promoter.

REMARKS

This amendment is in response to the Office Action dated July 27, 1989. Claims 1-18 remain for consideration.

Rejection under 35 U.S.C. §112

Claims 1, 4, 7, 10, 13 and 16-18 have been rejected under §112 for various reasons. Each of these rejections are traversed and reconsideration requested in view of the following remarks.

Claims 7, 10, 13 and 16 stand rejected under §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, claims 7 and 16 are asserted to be indefinite in their recitation of the phrase "by steps." Applicants have amended claims 7 and 16 to more clearly embrace embodiments

of the present invention. Claims 7 and 16 now clearly state that the plant cell or differentiated dicotyledonous plant of the present invention contain a chimeric gene comprising either the 35S or 19S promoter of CaMV.

Claim 10 has been asserted to be indefinite in its recitation of "region of homology" in that it fails to specify the object of homology which is being compared. While Applicants disagree with this rejection because the claim as presently written does specify that the region of homology is from *Agrobacterium tumefaciens* through the use of the conjunction "and" in line 2 of claim 10, Applicants have amended claim 10 to insert the reference to *Agrobacterium tumefaciens* immediately following the phrase "region of homology" and have deleted the conjunction "and" to remove any doubt as to the intended meaning. Claim 13 was asserted to be indefinite in its use of the word "modified." Applicants have deleted this word and in its place inserted the word "disarmed" which has a clear and definite meaning to those skilled in the art. The rejections to claims 10 and 13 should, therefore, also be withdrawn.

Claim 10 has been further rejected under §112, first paragraph, because it is asserted by the Patent Office that the disclosure is enabling only for claims limited to a plant transformation plasmid comprising the right T-DNA border. It is asserted by the Patent Office that it is well known in the art that the right T-DNA border is required for exogenous gene incorporation and that undue experimentation would be required by one of ordinary skill in the art to obtain stable foreign gene incorporation not utilizing the right border. This rejection is respectfully traversed and reconsideration requested. It must be understood that claim 10 pertains to an intermediate plant transformation plasmid and therefore needs to only have one border sequence which could be the right or left border since the acceptor plasmid would have the other border sequence. Therefore, there is no requirement that the right border sequence be associated with an intermediate plant transformation plasmid as claimed in claim 10.

Claims 16-18 stand rejected under §112, first paragraph, asserting that the disclosure is enabling only for claims limited to transformed dicots. Claim 16 has been amended to include a reference to dicotyledonous plants. While it may be true that monocot cells are more recalcitrant to plant regeneration than dicot cells, the promoter from cauliflower mosaic virus (35S or 19S) performs as a promoter of a heterologous gene in either monocots or dicots. It is only in the

regeneration of the monocots that difficulty is observed, not in the use of the promoter from CaMV to drive an inserted gene. In light of this amendment, this rejection should be removed.

Claims 1, 4, 7, 10, 13 and 16 have also been rejected under §112, first paragraph, under the assertion that the disclosure is enabling only for claims limited to the CaMV (19S) and (35S) promoters. These claims have been amended to clearly recite the use of only the CaMV35S or CaMV19S promoters. Therefore, this rejection has been obviated and should be removed.

Rejection under 35 U.S.C. §103

Claims 1-15 further stand rejected under §103 as being unpatentable over Anderson taken with Guilley et al. The Patent Office has taken the position that Anderson teaches plant cells transformed with DNA constructs comprising a viral promoter, a gene encoding the kanamycin resistance enzyme, portions of the CaMV genome, and T-DNA borders. As the Patent Office readily admits though, Anderson does not teach (heterologous) exogenous gene expression driven by the CaMV 35S or 19S promoters. Guilley et al. is asserted to teach the identification of the CaMV 35S and 19S promoters and their strength. The Patent Office asserts that it would have been obvious to one of ordinary skill in the art to utilize the method of T-DNA mediated plant transformation utilizing viral promoters as taught by Anderson and to incorporate the strong CaMV 35S and 19S promoters taught by Guilley since each would continue to function in its known and expected manner. The position of the Patent Office and rejection based on this position are respectfully traversed and reconsideration requested.

As is understood, this application is concerned primarily with a chimeric gene comprising a plant virus promoter from cauliflower mosaic virus coupled with a heterologous structural sequence and the expression of such a gene in a plant cell or differentiated plants. With this in mind, Applicants have claimed (in claims 1-3) a method for transforming a plant cell to express a chimeric gene where the improvement comprises a chimeric gene containing a promoter from CaMV selected from either the CaMV35S or CaMV19S promoter. Claims 4-6 claim the chimeric gene which is expressed in plant cells that comprises the CaMV35S or CaMV19S promoter and a structural sequence which is heterologous with respect to the promoter. Claims 7-9 claim a plant cell capable of expressing a

polypeptide by transcription of the chimeric gene as set forth in claims 4-6. Claims 10-12 claim an intermediate plant transformation vector that comprises a region of homology to *Agrobacterium tumefaciens*, a T-DNA border region from *Agrobacterium tumefaciens* and a chimeric gene as set forth in claims 4-6. Claims 13-15 claim a plant transformation vector comprising a disarmed plant tumor inducing plasmid of *Agrobacterium tumefaciens* which is capable of inserting a chimeric gene into susceptible plant cells where the chimeric gene is as described in claims 4-6. Finally, claims 16-18 claim a differentiated plant comprising plant cells containing a chimeric gene as described in claim 4. None of these claims as now amended are rendered obvious by the cited references.

As the Patent Office readily admits, Anderson does not teach, disclose or suggest a chimeric gene, intermediate plant transformation vector, plant transformation vector, plant cell or differentiated plant that includes a chimeric gene having a promoter from CaMV selected from the CaMV35S or CaMV19S promoter. Anderson only teaches plant cells transformed with a vector that includes a promoter from the Herpes Simplex Virus thymidine kinase gene. As is apparent, this promoter is not one that would normally include a plant cell as its host since it is a mammalian virus. It is also well-known to those skilled in the art that a viral promoter from a source that is not known to be functional in plants fails to express the gene to which it is coupled even if transferred into the plant cell. This has been stated in A. Caplan et al., "Introduction of Genetic Material into Plant Cells," Science, vol.222, pp.815-821 (1983) on page 818. A copy of this reference is enclosed with this response. This proposition is also further supported by the accompanying declaration of Dr. Stephen G. Rogers. Considering the erroneous nature of Anderson's teachings, there would be no reasonable expectation by one skilled in the art to use the 35S or 19S promoter from CaMV in a chimeric gene to obtain expression of a heterologous gene sequence transformed into a plant cell. Anderson never even mentions such a possibility. There is simply no suggestion whatsoever in Anderson to utilize a CaMV promoter in a transformation vector to obtain expression of a chimeric gene in plant cells. As the Federal Circuit Court of Appeals has stated on numerous occasions: "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching or suggestion that the combination be made." *See* In re Stencel, 4 U.S.P.Q.2d 1071,1073 (Fed. Cir. 1987). The primary issue in a determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that the invention

be carried out and that it would have a reasonable likelihood of success, viewed in light of the prior art. Anderson does not provide one skilled in the art with any suggestion that the use of the 35S or 19S promoter from CaMV would have any reasonable likelihood of success. When the prior art is viewed in relation to the present invention such a reasonable likelihood of success does not exist.

The Guilley et al. reference does not supply the missing suggestion that the 35S or 19S promoter from CaMV would be capable of driving the expression of a chimeric gene in a plant cell. Guilley only stands for the proposition that the 35S and 19S promoters exist in the CaMV and that they transcribe the CaMV DNA sequences at a relatively high level. There is no suggestion that the promoter could be coupled with a heterologous DNA sequence to obtain expression of the polypeptide for which the sequence codes in transformed plants. The Patent Office has combined these two references only for their individual teachings where no suggestion for the combination or that any reasonable likelihood of success existed that the combination would work. Other factors support the proposition that there was no reasonable likelihood of success that the invention of the instant application would work.

As stated in the Rogers' declaration, a recognized uncertainty to the successful isolation of a small fragment of the CaMV genome that contained a functional 35S or 19S transcript promoter was that a trans-acting protein encoded by CaMV may have been required for activity of the 35S promoter. If the fragment containing the promoter did not also produce the trans-acting protein, the promoter would have been inactive or active at a reduced level. The reason to think that other CaMV encoded proteins could have been essential for CaMV RNA synthesis came from other studies on bacteriophage and mammalian viruses. Studies of bacteriophage such as the coliphages T4 and T7 showed that these bacterial viruses produce proteins that are absolutely essential for the transcription of virus late genes. The virally encoded proteins are essential for transcription, and in the case of T7, the essential virus protein is an RNA polymerase that can recognize and use promoter sequences in the virus DNA. In the case of T4 phage, a new RNA polymerase is not made but a new protein accessory factor (called a sigma factor) that modifies the specificity of the host RNA polymerase is synthesized. The accessory protein allows the host polymerase to recognize and initiate mRNA synthesis at virus promoter sequences.

Virus encoded proteins have also been shown to be required for the expression of promoters and production of RNAs in mammalian viruses. The early and late genes of Herpes Simplex Virus require a class of proteins encoded by the virus, called E1 proteins, for their transcription. The E1 types of proteins are made and required by many different classes of viruses including HTLV. If the activator protein is not made, the level of subsequent RNA synthesis is much reduced.

The data from bacterial viruses and animal viruses suggest that the high level of transcription seen during infection of plants by CaMV might not be seen with chimeric gene constructs because of lack of a potentially required protein factor for optimal transcription. There was not enough known about the biology of CaMV in 1983 when the present application was filed to permit predictions as to whether such a protein factor was made by or necessary to the activity of CaMV promoters.

In view of the above remarks and the evidence presented in the Rogers' declaration, the §103 rejection on claims 1-15 should be withdrawn. Such action is respectfully solicited.

Claims 16-18 have been rejected under §103 as being unpatentable over Anderson taken with Guilley et al. as applied previously and further in view of Zambryski et al. Zambryski is asserted as teaching the regeneration of whole plants from cell transformed with a vector containing chimeric genes, T-DNA borders and deleted tumor genes. Nothing in Zambryski suggests a differentiated plant comprising a chimeric gene that includes a promoter selected from the CaMV35S or CaMV19S promoter. In light of the discussion above distinguishing Applicants' invention from the teachings of Anderson and Guilley, Zambryski does not add the sufficient teachings or suggestions to render Applicants' claimed invention obvious. Therefore it is believed that the §103 rejection as it pertains to claims 16-18 should be withdrawn. Such action is respectfully requested.

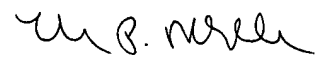
Applicants also wish to call the Examiner's attention to U.S. Patent No. 4,407,956 issued to Howell on October 4, 1983. This patent had been relied upon by the Patent Office in the parent of the instant application. Even though Applicants

call the Office's attention to Howell, it is not considered more relevant than those references currently cited by the Office in the Office Action of July 27, 1989. Howell only teaches the insertion of a foreign gene into the entire CaMV genome and then infecting plants with the CaMV to obtain expression of the foreign gene in plants. Nowhere is the 35S or 19S promoter from CaMV used as part of a chimeric gene to be inserted into plants.

A two-month extension of time extending the period to respond until December 27, 1989 accompanies this response. The extension of time is being filed in triplicate in that the appropriate fee is being charged to our deposit account.

In view of the foregoing remarks and amendments, it is now believed that this Application is in condition for formal allowance. Such action in the regular course of business is respectfully solicited. If the Examiner believes that a phone conference would be beneficial to the quick allowance of this case, he is requested to call Applicants' attorney at the number listed below.

Respectfully submitted,



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